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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/974,591	10/09/2001	John P. Alsobrook II	15966-654 CIP (Cura-154 C	7088

30623 7590 12/06/2004

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EXAMINER	
BRANNOCK, MICHAEL T	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 12/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/974,591	ALSOBROOK ET AL.	
	Examiner	Art Unit	
	Michael Brannock	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-14,27 and 30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-14,27 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *121101, 010603*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Status of Application: Claims and Amendments

Applicant is notified that the amendments put forth on 8/30/04, have been entered in full. Applicant's election, without traverse, of Group II, claims 5-14, 27, and 30, as the claims relate to a polynucleotide of SEQ ID NO: 13 is acknowledged. The instantly pending claims are directed to this elected in invention.

Information Disclosure Statement

The IDS filled Dec. 11, 2001 and Jan, 06, 2003 makes reference to certain partial international search reports, yet there is insufficient information contained in the citations so as to lead the reader to the required information. Therefore the information supplied by Applicant has been considered by the examiner, but the citations will not be printed on the face of the patent should a patent issue.

Priority

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). The specific reference to any prior nonprovisional application must include the relationship (i.e., continuation, divisional, or continuation-in-part) between the applications except when the reference is to a prior application of a CPA assigned the same application number.

Specifically, at line 7 of the specification serial number 60/323,755 is left blank. Also, the status of the 09/777,789 application is Abandoned.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 5-14, 27, and 30 are rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility. The claims are directed to polynucleotides encoding polypeptides of SEQ ID NO: 13 The instant specification puts forth that the polypeptide is useful in a screening method to determine what ligands may activate or inhibit the polypeptide and also to determine what the physiological effects of the polypeptide might be (see page 82 for example). This proposed use lacks a specific and substantial utility. It is not a specific use because any integral membrane protein could be used in exactly the same way. Further, many polypeptides are known in the art, yet the polypeptides have no known function or known ligands. Any of these orphan clones could be used in the manner described in the specification for the claimed polypeptide.

Furthermore, the proposed use of the polypeptide to screen for ligands of the polypeptide or for biologic effects of the polypeptide is not a substantial utility. A substantial utility is a practical use which amounts to more than a starting point for further research and investigation and does not require or constitute carrying out further research to identify or reasonably confirm what the practical use might ultimately be. For example, an assay that measures the presence of

a material which has a stated correlation to a predisposition to the onset of a particular disease condition would be a practical use of the material. However, a method of treating an unspecified disease or condition with a material that has no particular correlation with a disease would not constitute a substantial utility. Basic research, such as studying the properties of the claimed product or the mechanisms in which the product is involved, does not constitute a substantial utility.

The specification puts forth that the polypeptide could be involved in any number of disparate disease states, e.g. cardiovascular, endocrine, metabolic, neurologic, psychiatric, autoimmune, inflammatory and oncologic diseases, and could therefore be used as a diagnostic or therapeutic agent (see page 13, for example). A stated belief that a correlation exists between the polynucleotides or polypeptides and any number of diseases is not sufficient guidance to use the claimed polynucleotides to treat and/or diagnosis a particular disease; it merely defines a starting point for further research and investigation.

The specification puts forth that the polynucleotides and polypeptides could be used as tissue specific or chromosomal markers, page 87. Consistent with current examination guidelines, use as a tissue specific and/or chromosomal marker is not considered to be a substantial utility. Most every polypeptide exhibits some tissue specific pattern of expression and most every gene encoding a polypeptide is localized to some region of a chromosome. However, without some assertion that the tissue or chromosomal localization can be used to practice a particular substantial utility, as in a marker for a particular disease state, the use of the polypeptides or polynucleotides as tissue or chromosomal marker does not constitute a substantial utility.

The specification puts forth that the polypeptide and/or polynucleotides could be used in forensic biology (page 87). While one of skill in the art would appreciate that polymorphisms in the disclosed sequences must exist in any large population, this amounts to nothing more than an invitation to the skilled artisan to try and find such polymorphisms. Moreover, the specification does not teach that any particular nucleic acid or amino acid sequence is distinctive of any individual.

The specification puts forth that the polypeptide or polynucleotide could be used as part of a micro-array for toxicology testing and drug screening (see page 82). These purposed uses are not substantial utilities because each use amounts to no more than an invitation to study the properties of the polynucleotides or polypeptides, e.g. to determine whether a compound alters the expression of the polypeptide, and then to determine what, if any, the consequence of that alteration may be, or also to determine what ligands might bind to the polypeptide, e.g. drug screening. Such an invitation to perform research on the claimed polynucleotide is not a substantial utility.

The instant application has failed to provide guidance as to how one of skill in the art could use the claimed invention in a way that constitutes a specific or substantial utility. The proposed uses of the claimed invention are simply starting points for further research and investigation into potential practical uses of the claimed nucleic acids.

Claim 14 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claim is directed to a cell comprising an expression vector comprising SEQ ID NO: 13. The specification specifically contemplates the use of these vectors

in gene therapy, see page 80. Thus, the claims encompass the cells of a human patient and in a human patient that have been transfected and are thus not patentable.

Claims 5-14, 27, and 30 are also rejected under 35 U.S.C. § 112 first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention so that it would operate as intended without undue experimentation.

Furthermore, the claims encompass polynucleotides encoding polypeptide variants of the polypeptide of SEQ ID NO: 13, i.e. substitutions, deletions or insertions in a protein corresponding to SEQ ID NO: 14; should Applicant establish a specific and substantial utility for the claimed polynucleotides, Applicant has not provided sufficient guidance as to how to make and use the encoded polypeptides which are not 100% identical to the polypeptide of SEQ ID NO: 14, but which still retain a desired property of the polypeptide of SEQ ID NO: 14. The claims require polypeptides comprising only portions of SEQ ID NO: 14. The claims require polynucleotides encoding polypeptides having a recited degree of identity with SEQ ID NO: 14. Thus, the vast majority of polypeptides are amino acid sequence variants of SEQ ID NO: 14, i.e. amino acid substitutions, deletions or insertions in a protein corresponding to SEQ ID NO: 14, yet the specification has failed to teach one of skill in the art which amino acid substitutions, deletions or insertions to make. Furthermore, the Applicant has not provided guidance as to what properties of the allelic variants or sequence variants of the protein corresponding to SEQ ID NO: 14 might be desired nor any guidance as to which amino acid substitutions, deletions or

insertions to make to achieve any desired property. Applicant has not defined a difference in structure or difference in function between the protein corresponding to SEQ ID NO: 14 and variants of said protein. If a variant of the protein corresponding to SEQ ID NO: 14 is to have a structure and function similar to the protein corresponding to SEQ ID NO: 14, then the specification has failed to teach one of skill in the art which amino acid substitutions, deletions or insertions to make that will preserve the structure and function of the protein corresponding to SEQ ID NO: 14. Conversely, if a protein variant of SEQ ID NO: 14 need not have a disclosed property, the specification has failed to teach how to use such a variant.

The specification has failed to provide an activity of SEQ ID NO: 14 to be used to evaluate the claimed variants for usefulness. The specification has not provided a working example of the use of a variant of the polypeptide of SEQ ID NO: 14 nor sufficient guidance so as to enable one of skill in the art to make such a variant. The specification has failed to teach which amino acids of SEQ ID NO: 14 could be modified so as to produce a polypeptide that is not identical to SEQ ID NO: 14 and yet still retain the activity of the polypeptide of SEQ ID NO: 14 - which has apparently not been disclosed. Nor has any particular disorder been associated with the polypeptide or the polynucleotide such that one skilled in the art could make a pharmaceutical composition as in claims 27 and 30.

The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the

sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These regions can tolerate only relatively conservative substitutions or no substitutions (see Bowie et al., 1990, Science 247:1306-1310, especially p.1306, column 2, paragraph 2). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Also, these or other regions may be critical determinants of antigenicity. It is well appreciated in the art of antibody production that it is unpredictable which amino acids are critical antigenic determinants (see Alexander et al., Proc. Natl. Acad. Sci. 89(3352-3356)1992. Protein antigenicity can be significantly reduced by substitution of even a single residue. Further, even if an amino acid substitution does not destroy the activity of the immunizing protein, the substitution may significantly reduce the antigenicity of the protein (see the Abstract of Alexander et al.). The specification does not provide sufficient guidance as to how to make antibodies that are specific to variants of SEQ ID NO: 14 that can be used for any specific purpose. The specification has not provided guidance as to natural variants that may exist, nor how to use antibodies specific to variants that might be created.

Although the specification outlines art-recognized procedures for producing variants (e.g. page 44), this is not adequate guidance as to the nature of active variants that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the

specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity.

The specification has also failed to teach where to look for naturally occurring allelic variants of SEQ ID NO: 14, e.g. no disorder or phenotype has been asserted to correlate with a naturally occurring allelic variant, such that the artisan might now where to obtain a variant. The specification merely offers the skilled artisan the invitation to randomly try to find variants through trial and error sampling of animal populations.

Due to the large quantity of experimentation necessary to generate the infinite number of variant recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claims 5-14, 27, and 30 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses a polynucleotide of SEQ ID NO: 1, yet the claims encompass polynucleotides not described in the specification, i.e. polynucleotides which comprise only portions of SEQ ID NO: 1, e.g. sequences from other species, mutated sequences, allelic variants, or sequences that have a recited degree of identity. None of these sequences meet the written description provision of 35 U.S.C. 112, first paragraph. Although one of skill in the art would reasonably predict that these sequences exist, one would not be able make useful predictions as to the nucleotide positions or identities of those sequences based on the information disclosed in the specification.

The instant disclosure of a single polynucleotide, that of SEQ ID NO: 13 and a single silent nucleotide polymorphism, SEQ ID NO: 11, encoding a polypeptide with no instantly disclosed specific activities, does not adequately support the scope of the claimed genus, which encompasses a substantial variety of subgenera. A genus claim may be supported by a representative number of species as set forth in *Regents of the University of California v Eli Lilly & Co,* 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. The instant specification discloses, however, a single isolated polynucleotide sequence SEQ ID NO: 1, which is not sufficient to describe the essentially limitless genera encompassed by the claims.

The instant claims are not directed to that which is disclosed as essential to the invention, i.e. something that is homologous to the parent SEQ ID NO: 1 and has the function of the parent

polynucleotide. Thus, with the exception of the of the polynucleotides of SEQ ID NO: 11 and 13, and other polynucleotides which encode a polypeptide of SEQ ID NO: 14, the skilled artisan cannot envision encompassed variants. Therefore, only a polynucleotides encoding a polypeptide of SEQ ID NO: 14, and polynucleotides *consisting* of fragments thereof, or polynucleotides consisting of fragments thereof and heterologous sequences (e.g. carrier or tag sequences), but not the full breadth of the claims meet the written description provision of 35 U.S.C. §112, first paragraph.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 5-14are rejected under 35 U.S.C. 102(e) as being anticipated by US Published Application US20020132273 which is fully supported by US provisional application, 60198474, filed April 12, 2000.

US Published Application US20020132273 discloses polynucleotides encoding a polypeptide (SEQ ID NO:197) that has 96% sequence identity with the instant SEQ ID NO: 13, and would thus be considered an allelic variant, particularly due to the conservative substitution at position 194, see attached sequence alignment. Vectors and host cells and other variants are also taught, see paragraphs 0051 and 0088. SEQ ID NO: 197 is fully supported in prior application 60198474 where it is disclosed as AOLFR107 at page 104.

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US-09-886-055-197
; Sequence 197, Application US/09886055
; Patent No. US20020132273A1
; GENERAL INFORMATION:
;  APPLICANT: STRYER, LUBERT
;  APPLICANT:  ZOZULYA, SERGEY
;  TITLE OF INVENTION: RECEPTOR FINGERPRINTING, SENSORY PERCEPTION, AND
;  TITLE OF INVENTION:  BIOSENSORS OF CHEMICAL SENSANTS
;  FILE REFERENCE: 078003-0277150
;  CURRENT APPLICATION NUMBER: US/09/886,055
;  CURRENT FILING DATE:  2001-06-22
;  PRIOR APPLICATION NUMBER: 60/213,812
;  PRIOR FILING DATE: 2000-06-22
;  NUMBER OF SEQ ID NOS: 522
;  SOFTWARE: PatentIn Ver. 2.1
; SEQ ID NO 197
;   LENGTH: 316
;   TYPE: PRT
;   ORGANISM: Homo sapiens
US-09-886-055-197

  Query Match           96.8%;  Score 1606;  DB 9;  Length 316;
  Best Local Similarity  99.7%;  Pred. No. 5.5e-145;
  Matches  315;  Conservative    1;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          9 MELWNFTLGSGFILVGILNDSGSPELLCATITILYLLALISNGLLLLAITMEARLHMPMY 68
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MELWNFTLGSGFILVGILNDSGSPELLCATITILYLLALISNGLLLLAITMEARLHMPMY 60

Qy         69 LLLGQLSLMDLLFTSVVTPKALADFLRRENTISFGGCALQMFLALTMGGAEDLLLAFMAY 128
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 LLLGQLSLMDLLFTSVVTPKALADFLRRENTISFGGCALQMFLALTMGGAEDLLLAFMAY 120

Qy        129 DRYVAICHPLTYMTLMSSRACWLMVATSWILASLSALIYTVYTMHYPFCRAQEIRHLLCE 188
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 DRYVAICHPLTYMTLMSSRACWLMVATSWILASLSALIYTVYTMHYPFCRAQEIRHLLCE 180

Qy        189 IPHLLKLACADTSRYELMVYVMGVTFLIPSLAAILASYTQILLTVLHMPSNEGRKKALVT 248
              ||||||:||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 IPHLLKVACADTSRYELMVYVMGVTFLIPSLAAILASYTQILLTVLHMPSNEGRKKALVT 240

Qy        249 CSSHLTVVGMFYGAATFMYVLPSSFHSTRQDNIISVFYTIVTPALNPLIYSLRNKEVMRA 308
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 CSSHLTVVGMFYGAATFMYVLPSSFHSTRQDNIISVFYTIVTPALNPLIYSLRNKEVMRA 300

Qy        309 LRRVLGKYMLPAHSTL 324
              ||||||||||||||||
Db        301 LRRVLGKYMLPAHSTL 316
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Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Brannock, Ph.D., whose telephone number is (571) 272-0869. The examiner can normally be reached on Mondays through Fridays from 10:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, Ph.D., can be reached at (571) 272-0961.

Official papers filed by fax should be directed to (703) 872-9306. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

MB

11/22/04